

REMARKS

Claim 1 has been amended to incorporate the limitations of Claim 2. Claim 2 has accordingly been canceled. Claims 40-43 have been amended to depend from Claim 1 rather than canceled Claim 2. Claim 20 was canceled in a previous amendment. After entry of the above amendments, Claims 1, 3-10, 13-19 and 21-45 are pending.

The Applicants thank the Examiner for her reminder of the requirements for Amendment format under 37 CFR 1.121. However, Applicants disagree with her statement that the term “conjugate,” which was in Claim 1 as originally filed, was missing from Claim 1 in its most recently presented form. The Examiner’s insertion of the term “conjugate” in Claim 1 in the paragraph of the Office Action containing the Claim Rejections under 35 USC §112, was incorrect. Claim 1, as originally filed, and twice amended, refers to a first enzyme conjugate comprising a first enzyme, wherein at least some of the probes are bound to a second enzyme conjugate comprising the second enzyme. The Examiner’s insertion of the term “conjugate” after the phrase “comprising the second enzyme” is therefore incorrect.

Claim Rejections Under 35 USC §112

Claim 1 was rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

Claim 1 as amended recites that “at least some of the probes are bound to a first enzyme conjugate comprising the first enzyme *prior to contacting the surface layer of the solid support with the composition comprising the first chemiluminescent substrate*, and

wherein at least some of the probes are bound to a second enzyme conjugate comprising the second enzyme *prior to contacting the surface layer of the solid support with the composition comprising the second chemiluminescent substrate.*” The Official Action asserts that there is no support for the italicized subject matter. Support for the amendments, however, can be found in the specification at least at page 8, lines 1-13. Moreover, according to the specification, “the method . . . can further comprise contacting the support surface with a sample comprising first target molecules labeled with a first label and second target molecules labeled with a second label prior to contacting the support surface with the substrate composition” (page 8, lines 1-5). The specification also states “[t]he first target molecules can be labeled with the first enzyme to form the first enzyme conjugate and the second target molecules can be labeled with the second enzyme to form the second enzyme conjugate” (page 8, lines 5-7). The specification therefore clearly discloses contacting the probes on the surface with the first and second enzyme conjugates *prior to contacting the support surface with the substrate composition.* It is respectfully submitted that the above disclosure provides adequate written support for the indicated claim language. Moreover, contact of the support with the first and second enzyme conjugates would result in bonding of the probes to the target molecules of the first and second enzyme conjugates. Since this step is conducted prior to contact with the substrate composition, the probes would be bound to the first and second enzyme conjugates prior to contact with the composition comprising the first chemiluminescent substrate. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 24 and 40 are also rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not disclosed in the specification. This rejection is respectfully traversed.

The Official Action asserts that support for fluorescent labels *attached to the surface layer* cannot be found in the specification. The specification states that “. . . a control label can be attached to a discrete area on the support surface (page 15, lines 23-24). The specification also states that “. . . the control label may be any type of label including a . . . fluorescent label” (page 16, lines 9-11). It is respectfully submitted that the above disclosures provide adequate written support for the claim language. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 10-12 were also rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. This rejection is respectfully traversed.

First, Claims 11 and 12 have been canceled without prejudice or disclaimer. With respect to Claim 10, the specification incorporates by reference copending U.S. Patent Application Serial No. 10/462,742 (page 1, lines 7-10). The ‘742 application discloses arrays having spots spaced approximately 100 microns center to center (page 27 of the ‘742 application). This spacing corresponds to a spot density of 10,000/cm². The ‘742 application thus illustrates that spotted arrays having densities well in excess of 1,000 discrete areas per cm² as set forth in Claim 10 could be realized. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 1-19 and 21-45 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is respectfully traversed.

According to the Official Action, it is unclear whether the probes are bound to the enzyme conjugates throughout the method or whether the probes become bound to the enzyme conjugates at some point during the performance of one of the method steps. It is respectfully submitted that Claim 1 is sufficiently definite. Moreover, Claim 1 recites that the probes are bound prior to contact of the surface layer of the solid support with the composition comprising the first chemiluminescent substrate. The binding of the probes and enzyme conjugates is therefore clearly not an “active process step” in Claim 1. Claim 1, however, contains open ended “comprising” language. Thus, Claim 1 would encompass additional method steps including those involving the active step of binding the probes and the enzyme conjugates. Thus Claim 13, which depends from Claim 1, recites that the method further comprises contacting the surface layer with a sample comprising first target molecules labeled with a first label and second target molecules labeled with a second label prior to contacting the support surface with the composition comprising the first chemiluminescent substrate.

Claim 1 has been rejected under 35 U.S.C. §112, second paragraph, as allegedly lacking antecedent basis for the phrase “second enzyme”. This rejection is respectfully traversed.

Applicant’s respectfully point out that Claim 1 recites “a second enzyme” at line 9 of the claim (i.e., the claim recites “ contacting the surface layer of the solid support with a composition comprising a second chemiluminescent substrate capable of being activated by *a second enzyme*”). Additionally, the Official Action has once again stated that the term “conjugate” was improperly deleted from Claim 1. Applicants once again draw the Examiner’s attention to the fact that the term “conjugate” has not been removed

from this claim. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 3-4 and 7, which recite methods according to Claim 1, were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is respectfully traversed.

It is respectfully submitted that these claims, as written, clearly describe the *structure* of the solid support and not an active method step. The probes are *described* in these claims as “bound”. Claims 3-4 and 7 therefore clearly do not recite an active step of “binding”. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claim 31 was rejected under 35 U.S.C. §112, second paragraph, for allegedly being unclear as to whether or not the recitation of the sample refers to a “sample comprising first target molecules . . . and second target molecules” as recited in Claim 13, or whether it is a distinct sample.

Claim 31 has been amended to clarify that the sample referred to in the claim is the sample described in Claim 13. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claim Rejections Under 35 USC §102 and 35 U.S.C. §103(a)

Claim 1 has been amended to incorporate the limitations of Claim 2. Claim 2 originally depended from Claim 1. Accordingly, only those rejections pertaining to Claim 2 and claims dependent therefrom (i.e., Claims 8 and 40-43) are addressed below. The remaining rejections have been obviated by amendment.

Claims 1, 3-4, 13-15, 21, 29, and 31-32 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cheek, et al. (“Chemiluminescence Detection for Hybridization Assays on the Flow-Thru Chip, a Three-Dimensional Microchannel Biochip,” *Anal. Chem.* 73:5777-5783 (2001)) (hereinafter referred to as “Cheek”). Claims 25 and 27 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cheek as evidenced by U.S. Patent Application Publication 2004/0009529 A1 to Weimer, et al. (hereinafter referred to as “Weimar”). Each of the above rejections is respectfully traversed.

As set forth above, Claim 1 has been amended to incorporate the limitations of Claim 2. Claim 2 was not included in either of the above rejections. Accordingly, each of the above rejection has been obviated. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 2, 5, 28 and 44 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of U.S. Patent No. 6,068,979 to Akhavan-Tafti (hereinafter “the ‘979 patent”).

Claim 1 has been amended to recite that detecting chemiluminescent emissions on a two-dimensional solid support surface layer. As shown in Figure 1 of Cheek, the microchannel support comprises an ordered array of microchannels that connect the planar surfaces of the support. Accordingly, during an assay “. . . molecular interactions occur within the three-dimensional volume of ordered microchannels rather than at two-dimensional surfaces” (page 5778 of Cheek). Therefore, the assay described in Cheek and relied upon in the Official Action does not occur on a two-dimensional solid support

surface layer. The '979 patent does not remedy the above noted deficiency of Cheek. Moreover, the '979 patent is merely being relied upon in the Official Action for the disclosure of surfactant enhancers. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent in view of Akhavan-Tafti, "Chemiluminescent Detection of DNA in Low- and Medium-Density Arrays," *Clinical Chemistry* 44:2065-2066 (1998) (hereinafter "Akhavan-Tafti").

As acknowledged in the Official Action, the '979 patent fails to disclose a plurality of probes disposed on a surface layer at a density of at least 50 or at least 100 discrete areas per cm² (page 16 of the Official Action). In order to remedy this acknowledged deficiency of the '979 patent, the Official Action relies upon the Akhavan-Tafti reference which, according to the Official Action, discloses chemiluminescent detection of DNA in low and medium density array of 100 spots per cm² (pg. 19 of the Official Action). The method disclosed in the '979 patent, however, involves the use of a *chemiluminescent peroxidase substrate* as the first chemiluminescent substrate and a second different enzyme substrate (Abstract of the '979 patent). In contrast, Akhavan-Tafti is directed to the use of a specific alkaline-phosphatase substrate. Moreover, Akhavan-Tafti recites that "[k]ey to the success of the method was the rapid detection at room temperature afforded by Lumigen APS" (pg. 2066 of Akhavan-Tafti). Lumigen APS is a specific *alkaline-phosphatase* substrate (Fig. 1 of Akhavan-Tafti). In view of the above, it is respectfully submitted that one of ordinary skill in the art would not have

been motivated to combine the references in the manner set forth in the Official Action. In particular, it is respectfully submitted that one of ordinary skill in the art would not have been motivated to employ the array of Akhavan-Tafti, which is specified for use with a specific *alkaline-phosphatase* substrate, with the chemiluminescent detection method of the '979 patent which requires the use of a chemiluminescent *peroxidase* substrate and second different substrate. As set forth in the MPEP, a reference "... must be considered in its entirety, including portions that would lead away from the claimed invention." MPEP § 2141.02. It is respectfully submitted that the disclosure in Akhavan-Tafti that the "key to success" of the assay method was the use of a specific alkaline phosphatase substrate would lead one of ordinary skill in the art away from the proposed combination with the '979 patent which specifies the use of a peroxidase substrate. Reconsideration and withdrawal of this rejection is therefore respectfully requested.

In the "Response to Arguments" section of the Official Action, the Examiner asserts that "... while the method of [the '979 patent] involves the use of a peroxidase substrate as the first chemiluminescent substrate, the second chemiluminescent substrate used in the method is a substrate for a second enzyme ... preferably alkaline phosphatase". As set forth above, however, it is the teachings of the secondary reference (i.e., the Akhavan-Tafti article) which would lead away from the proposed combination. Moreover, the teachings of this reference would lead one away from using any substrate other than the Lumigen APS substrate with the arrays disclosed therein. The method disclosed in the '979 patent and relied upon in the Official Action requires the use of a substrate other than Lumigen APS. The Official Action is therefore proposing to

combine the method of the '979 patent, which requires the use of *chemiluminescent peroxidase substrate*, with the array of the Akhavan-Tafti article which is specified for use with a specific *alkaline-phosphatase* substrate.

There is also objective evidence of non-obviousness which further distinguishes the subject matter of the claims from the '979 patent and Akhavan-Tafti. Moreover, an unexecuted declaration under 35 U.S.C. §132 is submitted herewith. The executed declaration under 35 U.S.C. §132 will be filed in a Supplemental Response. As set forth in the attached Declaration, significant improvements in array performance can be realized by using a chemiluminescent enhancing material in a microarray format on a two-dimensional support surface. It is respectfully submitted that this evidence of non-obviousness further distinguishes the subject matter of the claims from the '979 patent and Akhavan-Tafti.

In view of the above, Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 8 and 40-42 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of the '979 patent as applied to Claims 2, 5, 28, and 44, and further in view of U.S. Patent No. 6,602,658 to Bronstein et al. (hereinafter "Bronstein"). This rejection is respectfully traversed.

Claim 8 originally depended from Claim 2. The subject matter of Claim 2 has been incorporated into Claim 1 and Claim 8 has been amended to depend from Claim 1. As set forth above, the combination of Cheek and the '979 patent does not teach or reasonably suggest the method of Claim 1. Further, Bronstein does not remedy the above

noted deficiencies of the combination of Cheek and the '979 patent. Moreover, Bronstein is only being relied upon in the Official Action for the timing of the addition of enhancers (page 19 of the Official Action). Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claim 43 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of the '979 patent as applied to Claims 2, 5, 28, and 44, and further in view of U.S. Patent No. 5,523,212 to Akhavan-Tafti et al. (hereinafter "the '212 patent").

Claim 43 originally depended from Claim 2. The subject matter of Claim 2 has been incorporated into Claim 1 and Claim 43 has been amended to depend from Claim 1. As set forth above, the combination of Cheek and the '979 patent fails to teach or reasonably suggest the method of Claim 1. Further, The '212 patent does not remedy the above noted deficiencies of the combination of Cheek and the '979 patent. Moreover, the '212 patent is only being relied upon in the Official Action for the disclosure of certain types of enhancers and additives (page 30 of the Official Action). Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claims 42-43 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent and Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and further in view of the '212 patent.

Claims 42 and 43 originally depended from Claim 2. The subject matter of Claim 2 has been incorporated into Claim 1 and Claims 42 and 43 have been amended to depend from Claim 1. As set forth above, the combination of the '979 patent and Akhavan-Tafti does not teach or reasonably suggest the method of Claim 1. Further, the

'212 patent does not remedy the above noted deficiencies of the combination of the '979 patent and Akhavan-Tafti. Moreover, the '212 patent is only being relied upon in the Official Action for the disclosure of certain types of enhancers and additives (page 32 of the Official Action). Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claim 8 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent and Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and further in view of Bronstein. This rejection is respectfully traversed.

Claim 8 originally depended from Claim 2. The subject matter of Claim 2 has been incorporated into Claim 1 and Claim 8 has been amended to depend from Claim 1. As set forth above, the combination of the '979 patent and Akhavan-Tafti does not teach or reasonably suggest the method of Claim 1. Further, Bronstein does not remedy the above noted deficiencies of the combination of the '979 patent and Akhavan-Tafti. Moreover, Bronstein is only being relied upon in the Official Action for the disclosure of the timing of the addition of enhancers (pages 33-34 of the Official Action). Reconsideration and withdrawal of this rejection is therefore respectfully requested.

Claim 7 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of Huang, "Detection of multiple proteins in an antibody-based protein microarray system," *Journal of Immunological Methods* 255:1-13 (2001) (hereinafter "Huang"). Claim 9 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of Akhavan-Tafti. Claims 16-19 were rejected under 35

U.S.C. §103(a) as allegedly being unpatentable over Cheek or, alternatively, the '979 patent in view of Akhavan-Tafti, and further in view of International Publication No. WO 01/73134 A2 to Wang (hereinafter "Wang"). Claims 22-23 and 30 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek or, alternatively, the '979 patent in view of Akhavan-Tafti and further in view of U.S. Patent No. 6,905,826 to Ferea et al. (hereinafter "the '826 patent"). Claim 24 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of International Publication No. WO 01/83814 A2 to Yang, et al. (hereinafter "Yang"). Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek, or, alternatively, the '979 patent in view of Akhavan-Tafti, and further in view of U.S. Patent No. 6,518,068 B1 to Gambini, et al. (hereinafter "Gambini"). Claim 34 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of Bronstein. Claim 35 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of Bronstein, as applied to Claim 34, or, alternatively, the '979 patent in view of Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and further in view of U.S. Patent No. 5,145,772 to Voyta et al. (hereinafter referred to as "Voyta"). Claim 36 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of Bronstein, or, alternatively, the '979 patent in view of Akhavan-Tafti and further in view of U.S. Patent No. 5,196,306 to Bobrow et al. (hereinafter "Bobrow"). Claims 37-38 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent in view of Akhavan-Tafti as applied to Claims 1-5, 7-, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44 above, and further in view of U.S. Patent No. 6,852,503 B1 to Clothier (hereinafter "Clothier"). Claim 37 was rejected under 35

U.S.C. §103(a) as allegedly being unpatentable over Cheek as applied to Claims 1, 3-4, 13-15, 21, 29 and 31-32, and further in view of Clothier. Claim 38 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheek in view of Clothier as applied to Claim 37, and further in view of the '979 patent. Claim 39 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent in view of Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and further in view of U.S. Patent No. 5,137,804 to Greene et al. (hereinafter "Greene"). Claim 27 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent in view of Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and as evidenced by Girotti, et al., "Chemiluminescent Immunoperoxidase Assay for the Dot Blot Hybridization Detection of Parvovirus B19 DNA Using a Low Light Imaging Device," *Analytical Biochemistry* 236:290-295 (1996) (hereinafter "Girotti") and U.S. Patent No. 5,650,099 to Akhavan-Tafti (hereinafter referred to as "the '099 patent"). Claim 25 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent in view of Akhavan-Tafti and as evidenced by Girotti, and U.S. Patent No. 6,045,727 to Akhavan-Tafti, et al. (hereinafter "the '727 patent"). Claims 6 and 33-34 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent and Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and further in view of Bronstein. Claim 24 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the '979 patent and Akhavan-Tafti as applied to Claims 1-5, 7, 9, 13-15, 21, 28-29, 31-32, 40-41, and 44, and further in view of U.S. Patent No. 5,843,666 to Akahavan-Tafti et al. (hereinafter "the '666 patent"). Each of the aforementioned rejection is respectfully traversed.

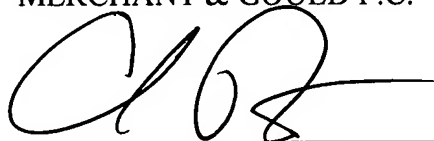
Claim 1 has been amended to incorporate the limitations of Claim 2 which originally depended from Claim 1. None of the aforementioned rejection include Claim 2 or a claim dependent from Claim 2 (i.e., Claims 8 and 40-43 originally depended from Claim 2). Accordingly, each of the above rejections has been obviated by amendment. Reconsideration and withdrawal of these rejections is therefore respectfully requested.

CONCLUSION

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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